

IN THE CLAIMS:

All claims currently pending and under consideration in the referenced application are shown in the listing of claims and will replace all prior versions and listings of claims in the application. Claims 12, 18 and 22 are amended herein. Claims 15-17 are cancelled. Claims 1-11, 13, 14, 19-21, 25 and 26 are withdrawn from consideration. No new matter has been added. All claim amendments are made without prejudice or disclaimer. Please amend the claims as follows:

Listing of the Claims:

1. (Withdrawn) An inhibitory peptide capable of inhibiting β pleated sheet formation in amyloid β -peptide said inhibitory peptide being a β sheet breaker peptide analog designed by chemical modification of a β sheet breaker peptide capable of inhibiting β pleated sheet formation in amyloid β -peptide.

2. (Withdrawn) The inhibitory peptide of claim 1 wherein said β sheet breaker peptide is a 5 residue Alzheimer inhibitor peptide iA β 5 (Leu-Pro-Phe-Phe-Asp SEQ ID NO:1).

3. (Withdrawn) An inhibitory peptide capable of inhibiting conformational changes in prion PrP protein associated with amyloidosis, said inhibitory being a β sheet breaker peptide analog designed by chemical modification of a β sheet breaker peptide capable inhibiting said conformational changes in prion PrP protein associated with amyloidosis.

4. (Withdrawn) The inhibitory peptide of claim 3 wherein said β sheet breaker peptide is 13 residue prion inhibitor peptide iPrP 13 (Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro Val, SEQ ID NO:2).

5. (Withdrawn) The inhibitory peptide of claim 4 wherein said chemical modification is achieved by a process selected from the group consisting of: alteration of the N- and C- terminal ends of said prion inhibitor peptide iPrP13; replacing at least one residue of said

prion inhibitor peptide iPrP13 with α -aminoisoburylic acid (Aib); methylation of the α carbon of at least one residue of said prion inhibitor peptide iPrP13 with a D-enantiomeric residue, forming head-to-tail cyclization of said prion inhibitor peptide iPrP13, replacing amide bonds in said prion inhibitor peptide iPrP13 with an amide bond surrogate; and combination thereof.

6. (Withdrawn) The inhibitory peptide of claim 5 wherein said alteration of the N- and C-terminal ends of said prion inhibitor peptide iPrP13 is achieved by a process selected from acetylation, amidation, desamination, alcoholization and combinations thereof.

7. (Withdrawn) The compound of claim 6 wherein said inhibitory peptide is selected from the group consisting of: ac-Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro Val-am, des-Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro Val-am, ac-Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro Val-alc, and des-Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro Val-alc.

8. (Withdrawn) The inhibitory peptide of claim 5 wherein said inhibitory peptide is selected from the group consisting of

Asp Ala Alb Ala Ala Aib Ala Gly Aib Ala Val Aib Val (SEQ ID NO: 4);

Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala (Me) Val Pro Val;

Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro (Me) Val;

Asp Ala Pro Ala Ala Pro Ala Gly Pro Ala (Me) Val Pro (Me) Val;

asp ala pro ala ala pro ala gly pro ala val pro val;

asp Ala Pro Ala Ala Pro Ala Gly Pro Ala Val Pro val;

asp Ala Pro ala Ala Pro ala Gly Pro ala Val Pro val;

Asp ψ [CH₂CH₂]Ala Pro ψ [CH₂CH₂]Ala Ala Pro ψ [CH₂CH₂]Ala Gly Pro ψ [CH₂CH₂]Ala ValPro ψ [CH₂CH₂]Val;

Asp ψ [CH₂S]Ala Pro ψ [CH₂S]Ala Ala Pro ψ [CH₂S]Ala Gly Pro ψ [CH₂S]Ala Val Pro ψ [CH₂S]Val;

Ac-Asp Ala Pro ψ [CH₂CH₂]Ala Ala Pro ψ [CH₂CH₂]Ala Gly Pro ψ [CH₂CH₂]Ala Val Pro Val-Am.

asp Ala Pro ψ [CH₂CH₂]Ala Ala Pro ψ [CH₂CH₂]Ala Gly Pro ψ [CH₂CH₂]Ala Val Pro val;

Ac-Asp Ala Proψ[CH₂S]Ala Ala Proψ[CH₂S]Ala Gly Proψ[CH₂S]Ala Val Pro Val-Am;
asp Ala Proψ[CH₂S]Ala Ala Proψ{CH₂S}Ala Gly Proψ[CH₂S]Ala Val Pro val;
Ac-Asp Ala Aib Ala Ala Aib Ala Gly Aib Ala Val Pro Val-Am (SEQ ID NO:5);
Ac-Asp Ala Proψ[CH₂CH₂]Ala Ala Proψ[CH₂CH₂]Ala Gly Proψ[CH₂CH₂]Ala Val Pro
(Me) Val;
Ac-Asp Ala pro Ala Ala Proψ{CH₂CH₂}Ala Gly pro Ala Val Pro Val-Am;
asp Ala Proψ[CH₂CH₂]Ala Ala Proψ[CH₂CH₂]Ala Gly Proψ[CH₂CH₂]Ala Val Pro (Me)
Val;
asp Ala Aib Ala Ala Proψ[CH₂CH₂]Ala Gly pro Ala Val Pro (Me) Val (SEQ ID NO:6);
asp Ala Aib Ala Ala Proψ[CH₂S]Ala Gly pro Ala Val Pro (Me) Val;
asp Ala Proψ{CH₂S}Ala Ala Proψ{CH₂S}Ala Gly Proψ[CH₂S]Ala Val Pro (Me) Val;
Ac-Asp Ala Aib Ala Ala Proψ[CH₂CH₂]Ala Gly Aib Ala Val Pro (Me) Val (SEQ ID
NO:7);

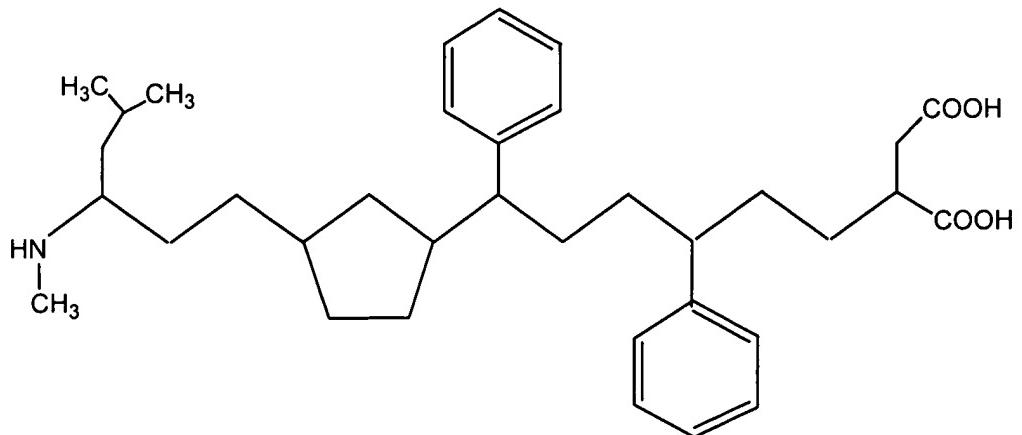
Asp Ala pro Ala Ala Proψ[CH₂CH₂] Ala Gly pro Ala Val Pro Val

Asp Al Aib Ala Ala Proψ[CH₂CH₂] Ala Gly Aib Ala (Me) Val Pro Val Pro Val

Ac-Asp Ala Proψ[CH₂S]Ala ala Proψ[CH₂S]Ala gly Proψ[CH₂S]Ala (Me) Val Pro
Val-Am;
Ac-Asp Ala Aib ala Ala Proψ[CH₂CH₂]Ala Gly pro Ala Val Pro (Me) Val;
asp Ala Aib Ala Ala Proψ[CH₂CH₂]Ala Gly Aib ala Val Pro Val-Am;
Ac-Asp Ala pro Ala Ala Proψ[CH₂CH₂]Ala gly pro Ala (Me) Val Pro Val-Am;
asp Ala Proψ[CH₂CH₂]Ala Ala Proψ[CH₂CH₂]Ala gly Proψ[CH₂CH₂]Ala val Pro val;
Ac-Asp Ala pro Ala ala Aib Ala gly pro Ala (Me) Val Pro Val-Am (SEQ ID NO:8);
Asp Ala pro Ala Ala Proψ[CH₂CH₂] Ala Gly pro Ala Val Pro Val;
Asp Ala Aib Ala Proψ[CH₂CH₂] Ala Gly Aib Ala (Me) Val Pro Val; and

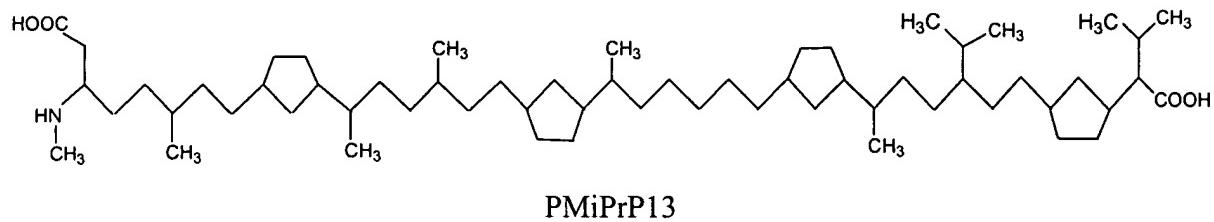
Asp Ala Pro Ala Ala Pro Ala Gly pro Ala Val Pro Val

9. (Withdrawn) A peptide mimetic with the following structure:



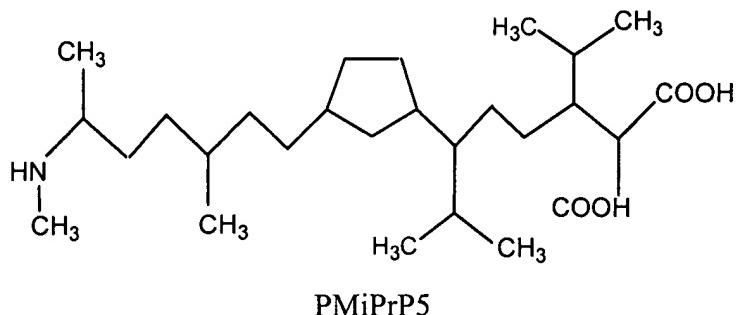
PMiA β 5

10. (Withdrawn) A peptide mimetic with the following structure:



PMiPrP13

11. (Withdrawn) A peptide mimetic with the following structure:

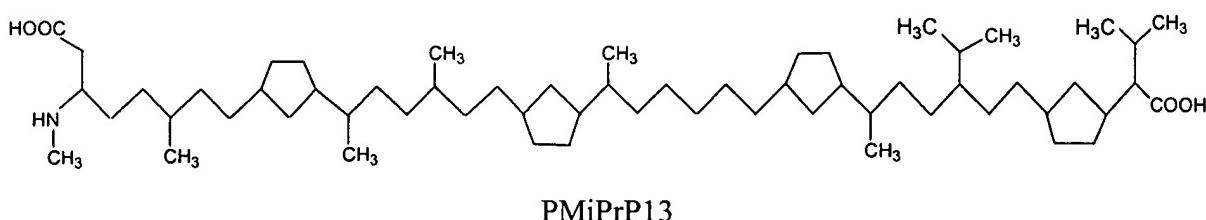
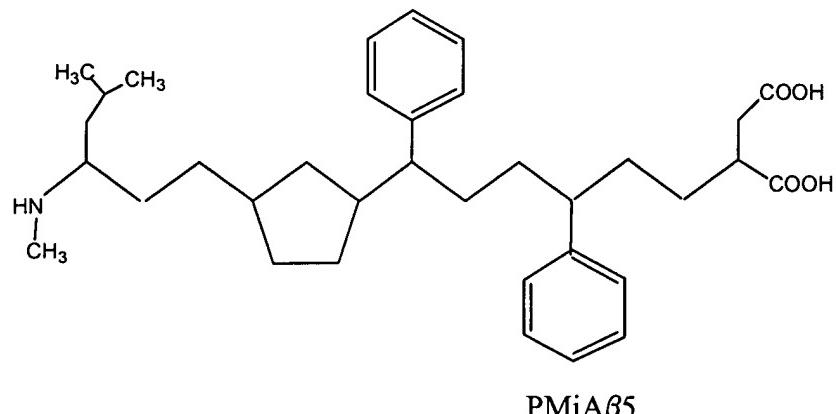


12. (Currently amended) A method for reducing the formation of amyloid or amyloid like deposits involving abnormal folding into β sheet structure of amyloid β peptide or for reducing the amount of said amyloid β peptide which has already formed into a beta sheet structure, the method comprising:

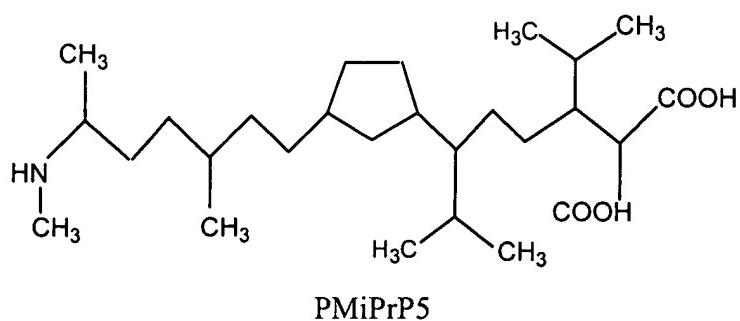
bringing into the presence of said amyloid β peptide either prior to or after the abnormal folding thereof into a β sheet structure, an effective amount of a β -sheet breaker peptide analog designed generated by chemical modification of a β -sheet breaker peptide consisting of SEQ ID NO: 1, capable of inhibiting β pleated sheet formation in an amyloid β peptide wherein the chemical modification of the β -sheet breaker peptide is achieved by a process selected from the group consisting of an altered N- or C- terminal end of the peptide; replacement of a residue of the peptide with α -aminoisobutyric acid (Aib); modification of an α carbon of the peptide selected from the group consisting of methylation, alkylation, dehydrogenation, and combinations of any thereof; amidation; replacement of an L-enantiomeric residue with a D-enantiomeric residue, head-to-tail cyclization of the peptide; replacement of an amide bond in the inhibitor peptide with an amide bond surrogate; and combinations of any thereof, and reducing the formation of amyloid or amyloid like deposits involving abnormal folding into β sheet structure of amyloid β peptide or reducing the amount of said amyloid β peptide which has already formed into a beta sheet structure.

13. (Withdrawn) A method for reducing the formation of amyloid or amyloid like deposits involving conformational changes in prion PrP protein or reducing the amount of said prion PrP protein which has already formed into amyloid or amyloid-like deposits comprising bringing into the presence of said prion PrP protein either prior to or after said conformational changes thereof into amyloid deposits an effective amount of the peptide of claim 3.

14. (Withdrawn) A method for reducing the formation of amyloid or amyloid like deposits by administration of a peptide mimetic selected from one of the group consisting of:



and



15. -17. (Cancelled).

18. (Currently amended) The method according to ~~claim 17~~ claim 12, wherein the alteration of the N- or C-terminal end is achieved by a process selected from acetylation, amidation, desamination, alcoholization and combinations thereof.

19. (Withdrawn) The method according to claim 12, further comprising:
administering an effective amount of a five residue inhibitor peptide analog to a subject, wherein the five residue inhibitor peptide analog has side-chain groups of amino acids Leu, Pro, Phe, Phe, and Asp, wherein the five residue inhibitor peptide analog further comprises a modification selected from the group consisting of: an altered N- or C-terminal end; replacement of a residue with α -aminoisobutyric acid (Aib); methylation of an α carbon; alkylation of an α carbon; dehydrogenation of an α carbon; amidation; replacement of an L-enantiomeric residue with a D-enantiomeric residue, head-to-tail cyclization; replacement of an amide bond with an amide bond surrogate; and combinations thereof; and
reducing the formation or amount of amyloid deposits involving an amyloid β peptide folding into a β sheet structure.

20. (Withdrawn) The method according to claim 19, wherein the alteration of the N- or C-terminal end is achieved by a process selected from acetylation, amidation, desamination, alcoholization and combinations thereof.

21. (Withdrawn) The method according to claim 19, wherein at least 81.5% of the five residue inhibitor peptide analog remains uncleaved when incubated *in vitro* with human microsomes at 37 °C for one hour.

22. (Currently amended) A method for reducing formation or amount of an amyloid deposit involving an amyloid folding into a β sheet structure, the method comprising: contacting the amyloid peptide, either prior to or after the abnormal folding thereof into a β sheet structure, with a means for reducing the formation or amount of an amyloid deposit, wherein the means for reducing the formation or amount of an amyloid deposit is a pharmaceutically composition comprising an effective amount of a β -sheet breaker peptide analog and a pharmaceutically acceptable carrier or vehicle, wherein the β -sheet breaker peptide analog is generated by chemical modification of a β -sheet breaker peptide consisting of SEQ ID NO: 1, wherein the chemical modification of the β -sheet breaker peptide is achieved by a process selected from the group consisting of an altered N- or C-terminal end of the peptide; replacement of a residue of the peptide with α -aminoisobutyric acid (Aib); modification of an α carbon of the peptide selected from the group consisting of methylation, alkylation, dehydrogenation, and combinations of any thereof; amidation; replacement of an L-enantiomeric residue with a D-enantiomeric residue, head-to-tail cyclization of the peptide; replacement of an amide bond in the inhibitor peptide with an amide bond surrogate; and combinations of any thereof, and reducing the formation or amount of an amyloid deposit involving an amyloid folding into a β sheet structure.

23. (Previously presented) The method according to claim 22, comprising administering the means for reducing the formation or amount of an amyloid deposit to a subject believed to suffer from a disease selected from the group consisting of Alzheimer's disease, Down's syndrome, Primary systemic amyloidosis, Secondary systemic amyloidosis, Familial Mediterranean fever, Creutzfeldt-Jakob disease, Gerstmann-Strausslet-Scheinker syndrome, Senile systemic amyloidosis, Familial amyloid polyneuropathy, Hemodialysis-related amyloidosis, and Hereditary cerebral amyloid angiopathy.

24. (Previously presented) The method according to claim 22, wherein the disease is Alzheimer's disease.

25. (Withdrawn) A method of detecting a amyloid β based disease in a subject, the method comprising:

administering a five residue peptide analog to a subject, wherein the five residue inhibitor peptide analog has side-chain groups of amino acids Leu, Pro, Phe, Phe, and Asp, wherein the five residue inhibitor peptide analog further comprises a modification selected from the group consisting of: an altered N- or C- terminal end; replacement of a residue with α -aminoisobutyric acid (Aib); methylation of an α carbon; alkylation of an α carbon; dehydrogenation of an α carbon; amidation; replacement of an L-enantiomeric residue with a D-enantiomeric residue, head-to-tail cyclization; replacement of an amide bond with an amide bond surrogate; and combinations thereof;

binding the five residue peptide analog to an amyloid β peptide in the subject; and visualizing binding of the five residue peptide analog.

26. (Withdrawn) The method according to claim 25, wherein visualizing binding comprises visualizing a fibril deposit.

27. (New) The method of claim 12, wherein the β -sheet breaker peptide analog is selected from the group consisting of

Ac-Leu Pro ψ [CH₂CH₂]Phe Phe Asp-Am

Ac-Leu Pro ψ [CH₂S]Phe Phe Asp-Am

(Me)Leu Pro ψ [CH₂CH₂]Phe Phe Asp-Am

leu Pro ψ [CH₂CH₂]Phe Phe asp

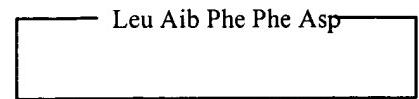
leu Pro ψ [CH₂S]Phe Phe asp

Ac-Leu Aib Phe Phe Asp-Am

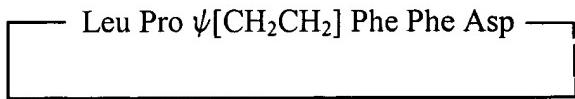
(Me)Leu Aib Phe Phe Asp-Am

Leu Pro ψ [CH₂CH₂]Phe Phe asp

Leu Aib Phe Phe Asp



Leu Pro ψ [CH₂CH₂] Phe Phe Asp



Ac-Leu pro Phe Phe Asp-Am

Ac-Leu Pro ψ [CH₂CH₂]Phe phe Asp-Am

Ac-Leu Pro ψ [CH₂S]Phe phe Asp-Am

Ac-Leu Pro ψ [CH₂CH₂]Phe (Me)Phe Asp-Am

Ac-Leu Pro ψ [CH₂CH₂]Phe (Me)Phe asp

Ac-Leu Pro phe phe Asp-Am

Ac-Leu Pro (Me)Phe phe Asp-Am

leu Pro ψ [CH₂CH₂]Phe phe asp

leu Pro (Me)Phe phe asp

Ac-Leu Aib Phe phe Asp-Am

28. (New) The method of claim 22, wherein the β -sheet breaker peptide analog is selected from the group consisting of

Ac-Leu Pro ψ [CH₂CH₂]Phe Phe Asp-Am

Ac-Leu Pro ψ [CH₂S]Phe Phe Asp-Am

(Me)Leu Pro ψ [CH₂CH₂]Phe Phe Asp-Am

leu Pro ψ [CH₂CH₂]Phe Phe asp

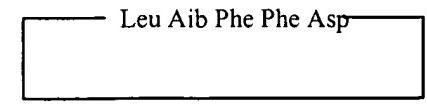
leu Pro ψ [CH₂S]Phe Phe asp

Ac-Leu Aib Phe Phe Asp-Am

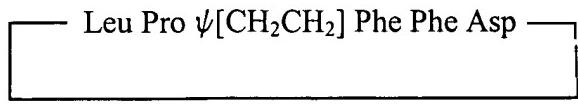
(Me)Leu Aib Phe Phe Asp-Am

Leu Pro ψ [CH₂CH₂]Phe Phe asp

Leu Aib Phe Phe Asp



Leu Pro ψ [CH₂CH₂] Phe Phe Asp



Ac-Leu pro Phe Phe Asp-Am

Ac-Leu Pro ψ [CH₂CH₂]Phe phe Asp-Am

Ac-Leu Pro ψ [CH₂S]Phe phe Asp-Am

Ac-Leu Pro ψ [CH₂CH₂]Phe (Me)Phe Asp-Am

Ac-Leu Pro ψ [CH₂CH₂]Phe (Me)Phe asp

Ac-Leu Pro phe phe Asp-Am

Ac-Leu Pro (Me)Phe phe Asp-Am

leu Pro ψ [CH₂CH₂]Phe phe asp

leu Pro (Me)Phe phe asp

Ac-Leu Aib Phe phe Asp-Am